In the United States Court of Federal Claims

OFFICE OF SPECIAL MASTERS

Case No. 11-140V

Filed: March 31, 2014

* *	**PUBLISHED**
SHERRY SALMINS, *	
*	Special Master Dorsey
Petitioner, *	
v. *	Entitlement; Human papillomavirus ("HPV") vaccine; Gardasil; Guillain-Barré syndrome ("GBS")
*	
*	
SECRETARY OF HEALTH *	
AND HUMAN SERVICES, *	
*	
Respondent. *	
* *	

Christina Ciampolillo, Conway, Homer & Chin-Caplan, P.C., Boston, MA, for petitioner.
Gordon Shemin, U.S. Department of Justice, Washington, DC, for respondent.

RULING ON ENTITLEMENT[1]

I. Introduction

On March 7, 2011, Sherry Salmins ("petitioner") filed a petition for compensation under the National Vaccine Injury Compensation Program ("the Program"),[2] in which she alleged that the human papillomavirus ("HPV") vaccine (Gardasil) she received on January 27, 2009, caused her to suffer from Guillain-Barré syndrome ("GBS"). Petition at 1. Petitioner filed an amended petition on July 18, 2011, which contained the same assertion. Amended Petition at 1.

[1] Because this published ruling contains a reasoned explanation for the action in this case, the undersigned intends to post this decision on the website of the United States Court of Federal Claims, in accordance with the E-Government Act of 2002 § 205, 44 U.S.C. § 3501 (2006). In accordance with the Vaccine Rules, each party has 14 days within which to request redaction "of any information furnished by that party: (1) that is a trade secret or commercial or financial in substance and is privileged or confidential; or (2) that includes medical files or similar files, the disclosure of which would constitute a clearly unwarranted invasion of privacy." Vaccine Rule 18(b); 42 U.S.C. § 300aa-12(d)(4)(B)(2006). Further, consistent with the rule requirement, a motion for redaction must include a proposed redacted ruling. If, upon review, the undersigned agrees that the identified material fits within the requirements of that provision, such material will be redacted.

[2] The Program comprises Part 2 of the National Childhood Vaccine Injury Act of 1986, 42 U.S.C. §§ 300aa-10 et seq. (2012). Hereafter, individual section references will be to 42 U.S.C. § 300aa.

Respondent recommended against compensation, stating that petitioner has not presented preponderant evidence that the vaccination caused her injuries. See Respondent's Rule 4 Report ("Resp't's Report"), filed Aug. 31, 2011, at 1, 13.

The parties submitted expert reports in support of their respective positions. Petitioner filed two reports from Nizar Souayah, M.D. Petitioner's Exhibits ("Pet'r's Ex.") 22 and 24. Respondent filed a report from Thomas Leist, M.D. Respondent's Exhibit ("Resp't's Ex.") A.

A hearing was held on August 21, 2013, during which the parties' experts testified. Respondent filed a post-hearing brief on December 9, 2013, and petitioner filed a post-hearing brief on January 9, 2014. The matter is now ripe for adjudication.

After a review of the entire record, § 300aa-13(a)(1), the undersigned finds that petitioner has provided preponderant evidence that her HPV vaccine caused her GBS, which satisfies her burden of proof under Althen v. Sec'y of Health & Human Servs., 418 F.3d 1274, 1280 (Fed. Cir. 2005). See Capizzano v. Sec'y of Health & Human Servs., 440 F.3d 1317, 1324 (Fed. Cir. 2006) (circumstantial evidence may satisfy a petitioner's burden of proof). Accordingly, petitioner is entitled to compensation.

II. Factual Background

A. Issues to Be Decided

Prior to the hearing, the parties filed a joint submission "identifying: (1) stipulated facts; (2) facts in dispute; (3) issues not in dispute; and (4) issues remaining to be resolved." Joint Prehearing Submission, filed July 2, 2013, at 1 (quoting Prehearing Order, filed Mar. 13, 2013).

The parties stipulate that petitioner received her HPV vaccine on January 27, 2009,[3] and that the HPV vaccine is listed on the Vaccine Injury Table (42 C.F.R. § 100.3). Id. The parties also stipulate that petitioner timely filed her petition and that she has suffered the residual effects of her alleged vaccine injury for more than six months. Id. at 1-2.

The issues that the parties dispute are, first, whether petitioner had GBS and, second, whether petitioner suffered GBS as a result of her HPV vaccine. Id. at 2. The parties stipulate that all other facts material to petitioner's proof of causation to which they did not specifically stipulate remain in dispute. Id.

B. Summary of Facts

At the time petitioner received the vaccination at issue in this case, she was 26 years old. Pet'r's Ex. 1 at 3. Her past medical history included diagnoses of polycystic ovarian syndrome ("PCOS") and infertility. Pet'r's Ex. 9 at 221; Pet'r's Ex. 2 at 1. Petitioner underwent an endoscopic thoracic sympathectomy in 1999 for excessive sweating of her hands. Pet'r's Ex. 9

[3] In their stipulation, the parties inadvertently stated that petitioner received her HPV vaccine on "January 7, 2009," instead of January 27, 2009.

at 221; Pet'r's Ex. 1 at 34. Petitioner gave birth to twin girls on October 30, 2007. Pet'r's Ex. 9 at 33.

On June 11, 2008, petitioner was seen for complaints of no menstrual period for five months and weight gain. Pet'r's Ex. 1 at 18. She was diagnosed with amenorrhea (no menses) related to her PCOS. Id. at 19. Treatment with oral contraception was discussed with petitioner. Id.

On January 27, 2009, at the office of Tracy Verrico, D.O., petitioner requested the Gardasil vaccine. Id. at 20. The Gardasil vaccine was administered to petitioner in her left deltoid intramuscularly. Id. at 21. Two days later, on January 29, 2009, at 11:30 a.m., petitioner called Dr. Verrico's office to report complaints of fatigue and flu-like symptoms since her HPV vaccination. Pet'r's' Ex. 1 at 22; Pet'r's Ex. 10 at 3. The note in Dr. Verrico's records regarding the telephone call from petitioner stated

> T.C. – Patient called with complaints of fatigue and feeling "flu like" since Gardasil administration on 1/27/09 – Initially had diarrhea times 2 approximately few hours after injection, then felt fatigue, chills, aches and feels tingling in her feet – lower legs. Temp: 98.4. Merck advised.

Pet'r's Ex. 1 at 22; see also Pet'r's Ex. 10 at 3.

Another note in Dr. Verrico's office records, also dated that same day, January 29, 2009, indicated that Dr. Verrico, or someone in the office, spoke with petitioner and then documented, "[f]lu like symptoms . . . improving. Tingling in lower extremities. Reviewed Adverse Reactions as listed with vaccine. Advised patient to come in if symptoms worsen and to not continue 2 and 3 vaccine." Pet'r's Ex. 1 at 23. A nurse from Dr. Verrico's office completed a Vaccine Adverse Event Reporting System ("VAERS") report. Id. at 3.

On February 1, 2009, petitioner again called Dr. Verrico complaining of "numbness extending to both thighs after driving > 1 hour." Id. at 23. At that time, petitioner had no motor symptoms and no upper respiratory symptoms. Id. Dr. Verrico "[a]dvised [petitioner] . . . to see [a] neurologist ASAP or to [go to the emergency department] if [symptoms] worsen." Id.

On February 2, 2009, petitioner presented to the emergency department ("ED") at Hackensack University Medical Center ("HUMC") with complaints of "extremity weakness" and "tingling." Pet'r's Ex. 14 at 5. Petitioner was seen by Deborah Hutter, M.D., who noted that petitioner had "received a Gardasil vaccination, and subsequently [had] fevers and diarrhea . . . [and] continued to have malaise and subsequently developed increased numbness." Id. at 13. On examination, petitioner reported "right greater than left numbness and weakness." Id. Dr. Hutter's diagnosis was "mild Guillain-Barre secondary to vaccination." Id. at 14. Dr. Hutter contacted Robert Angels, M.D., for a neurology consultation. Id.

Dr. Angels performed the neurology consultation that day, February 2, 2009. Like Dr. Hutter, Dr. Angels documented petitioner's history as follows:

> [Petitioner] received [the HPV vaccine] on [January 27, 2009]. Several hours later she developed flu-like symptoms marked by the development of malaise as well as diarrhea. She stated that the flu-like symptoms continued for approximately 24 hours. She denied the development of fever. By the following day, she had developed numbness and paresthesias initially involving her distal lower extremities extending proximally to the shin. By the following day, the paresthesias had extended proximally to approximately the level of the knee. One day later, the paresthesias extended to the thigh region, as well as to the upper extremities (right greater than left)…She has not developed any actual motor weakness. She is able to ambulate unassisted and she has no difficult[y] rising from a chair…She denies any difficulty with respiratory function or shortness of breath.

Pet'r's Ex. 12 at 21.

Dr. Angels noted that petitioner's motor, gait, and coordination were normal. Id. at 22. Petitioner had slightly diminished sensation in her right arm, and she complained of paresthesia of all extremities. Id. But she had no significant weakness. Dr. Angels suspected that petitioner had a "possible mild case of GBS." Pet'r's Ex. 13 at 211. Dr. Angels was hesitant to order IVIG treatment because petitioner had no motor dysfunction or weakness. Pet'r's Ex. 12 at 22. Dr. Angels instructed petitioner to follow up in two days and if she developed motor involvement, then he planned to initiate IVIG treatment. Id. He instructed petitioner to call his office or go to the ED if she developed any motor dysfunction or weakness, or if she developed respiratory problems or shortness of breath. Id. Petitioner was then discharged from the ED.

On February 5, 2009, petitioner returned to HUMC due to bilateral leg weakness, progressing over several days. Pet'r's Ex. 13 at 56. She had asymmetrical weakness in her lower extremities. Id. Deep tendon reflexes (DTRs) were 1+ in the upper extremities, 1+ at the knee, and 1 to 1- at the ankles. Id. Dr. Angels diagnosed petitioner with GBS that had worsened over 48 hours and ordered IVIG therapy. Id.

On February 6, 2009, Dr. Hutter noted that petitioner had "[m]ild Guillain Barre secondary to vaccination" and recommended that IVIG treatment continue. Id. at 62. On that same day, Dr. Angels performed a lumbar puncture. Id. at 51. The results of petitioner's cerebrospinal fluid ("CSF") test were normal. Pet'r's Ex. 12 at 18; Pet'r's Ex. 13 at 144. There was no growth of bacteria found in routine cultures and a Lyme antibody screening test was negative. Pet'r's Ex. 12 at 20; Pet'r's Ex. 13 at 166.

By February 7, 2009, petitioner was unable to ambulate without assistance. Pet'r's Ex. 13 at 189. Dr. Angels's diagnosis was "[p]robable GBS." Id. at 50. An MRI performed on February 9, 2009, was normal. Pet'r's Ex. 12 at 10, 27. Dr. Angels noted that petitioner's symptoms had not worsened, but she was still unable to ambulate. Pet'r's Ex. 13 at 47. His diagnosis remained "[p]robable GBS related to recent vaccine." Id. On February 10, 2009, petitioner completed the five-day course of IVIG treatment per Dr. Angels's order. See id. at 45. Dr. Angels's diagnosis on that date was GBS. Id.

On February 10, 2009, petitioner was transferred to the Kessler Institute of Rehabilitation ("Kessler") for rehabilitation of her ambulatory deficits. Pet'r's Ex. 8 at 7. On admission to

Kessler, petitioner was evaluated by Uri Adler, M.D. Dr. Adler noted that petitioner had been diagnosed with GBS and that she had received the Gardasil vaccination on January 27, 2009. Id. at 9. Petitioner lacked reflexes and had generalized weakness. Id. Dr. Adler's impression was that petitioner had GBS. Id. at 12; see also id. at 16. Dr. Adler stated that petitioner would be admitted for an inpatient comprehensive interdisciplinary rehabilitation program. Id. at 9-13. Petitioner, however, expressed that she was feeling depressed and wanted to be discharged. Id. at 7. She agreed to stay overnight for a physical therapy evaluation the next morning so that she could be properly set up for her discharge home. Id. In the morning, she was evaluated and discharged home with instructions for use of a cane, a prescription for Neurontin, and instructions for outpatient therapy. Id. at 7, 9-13. Petitioner was instructed to report to Dr. Angels if she experienced any symptoms of respiratory insufficiency or worsening weakness. Id. at 7. Dr. Adler's discharge diagnosis on February 12, 2009, was GBS. Id.

On February 13, 2009, nurse Kim Baker in Dr. Verrico's office completed the Merck VAERS report, in which she stated that petitioner began experiencing the adverse effects of the HPV vaccine a few hours after the administration of the vaccine on January 27, 2009. Pet'r's Ex. 10 at 2. An updated VAERS report was completed by Merck on April 7, 2009. Pet'r's Ex. 14 at 22-23. The report indicated that petitioner had not recovered. Id.

Petitioner received outpatient therapy from February 12, 2009, to March 2009. See Pet'r's Exs. 16 and 17. She presented to Dr. Angels in April 2009 for follow-up and reported that she had been to physical rehabilitation and outpatient therapy. Pet'r's Ex. 12 at 4. Petitioner was "nearly back to [normal]," and her paresthesias had resolved, but she felt fatigued. Id.

On June 9, 2009, petitioner was seen by Carl Saphier, M.D., for prenatal care and first trimester pregnancy screening. Pet'r's Ex. 5 at 43-44. Dr. Saphier noted that petitioner "developed [GBS] . . . 3 days after receiving the first injection of the HPV vaccine." Id. at 43. Petitioner reported residual left foot numbness. Id. Dr. Saphier recommended a neurological evaluation if petitioner developed any possibly related symptoms, such as increasing muscle weakness. Id. at 44. He ordered monitoring of fetal growth by serial ultrasound exams. Id.

Petitioner followed up with Dr. Angels on June 10, 2009. Pet'r's Ex. 12 at 1. She reported numbness in her left foot, which had begun 4.5 weeks prior. Id. Petitioner also reported occasional sharp, shooting pain in various muscles of her thigh, leg and calf. Id.

On September 25, 2009, petitioner was seen by Olga Noskin, M.D., for a neurological consultation. Pet'r's Ex. 3 at 8; Pet'r's Ex. 11 at 1. Dr. Noskin observed that petitioner was diagnosed with "what was thought to be [GBS] . . . back in February 2009 after the Gardasil vaccination." Pet'r's Ex. 11 at 1. Dr. Noskin noted that petitioner was pregnant and experiencing pain in her joints, especially in her wrists and elbows, since becoming pregnant. Id. Upon examination, Dr. Noskin noted that petitioner had some "give-way weakness in the lower extremities" but that the finding was normal. Id. at 2. Dr. Noskin's diagnosis was "[l]ower extremity distal sensory neuropathy possibly due to sequela from her Guillain-Barré syndrome versus pregnancy related." Id. Dr. Noskin planned to review petitioner's recent blood work and recommended that petitioner undergo a nerve conduction velocity study after she delivered her

baby. Id. Dr. Noskin also planned to see petitioner for a follow-up visit in approximately three months. Id.

Petitioner periodically saw Dr. Saphier from June 2009 through October 2009 for prenatal care. Pet'r's Ex. 4 at 17-34; Pet'r's Ex. 5 at 19-47. On November 20, 2009, petitioner was seen in the ED at Holy Name Hospital for contractions. Pet'r's Ex. 9 at 162. Petitioner was sent home but returned the next day and was admitted for recurrent contractions with a past medical history noted for "Guillain Barre [secondary] to Gardasil vaccine." Id. A preoperative progress note from November 21, 2009, stated that petitioner had a history of GBS with residual numbness. Id. at 170. Petitioner had a repeat caesarean section on November 21, 2009. Id. at 173. She was discharged on November 25, 2009. Id. at 180.

On February 5, 2010, when petitioner was 9 weeks postpartum, she presented to Dr. Noskin with complaints of pain and burning of her hands and feet. Pet'r's Ex. 3 at 3. Dr. Noskin noted in the neurological evaluation that petitioner had a

> history of Guillain-Barre syndrome s/p IVIG a year ago with residual painful paresthesis in her extremities. Reportedly, she had a normal spinal tap and, possibly, an abnormal EMG but those records were not made available to me. She has given birth a few months ago and feels that her pain has worsened and involves the legs up to her knees as well as hands. She thinks her hands are also somewhat weak.

Id. A review of petitioner's systems was positive for joint and muscle pain. Id. at 4. Her muscle strength and tone were normal except for weakened grips bilaterally. Id. Dr. Noskin's assessments were "[p]olyneuropathy . . .[c]hronic inflammatory demyelinating polyneuritis ["CIDP"] . . . [and] [a]utonomic dysreflexia." Id.

Dr. Noskin also noted that

> [petitioner's] symptoms are peculiar and the possibility of CIDP needs to be excluded. Because of the unclear diagnosis of GBS in the past and her continued symptoms, I need to perform a nerve conduction velocity test as well as a lumbar puncture to rule out the possibility of CIDP or a severe neuropathy.

Pet'r's Ex. 3 at 4. Petitioner was started on Lyrica for the neuropathy symptoms. Id.

Electrodiagnostic testing on February 9, 2010, was normal. Id. at 12-13. Another electrodiagnostic test performed on February 25, 2009, was also normal, with no evidence of polyneuropathy or demyelination. Id. at 11.

On March 1, 2010, petitioner presented to Dr. Noskin for complaints of numbness in her feet. Pet'r's Ex. 15 at 1. Dr. Noskin noted that petitioner's nerve conduction, CSF, and electromyography ("EMG") tests were all normal. Id.

On July 22, 2011, petitioner presented to HUMC due to a three-week history of numbness and tingling in her arms and legs. Pet'r's Ex. 20 at 4. Victoria Kou, M.D., noted

petitioner's "past history [of] GBS 2 years ago with chronic paresthesias and extremity weakness, now worse over last 3 weeks." Id. at 6. While in the ED at HUMC, petitioner was seen by neurologist Ann Miller, M.D. Id. at 7-9. Dr. Miller noted petitioner's past diagnosis of GBS, id. at 7, but she did not believe that petitioner had "active neurological disease" and ordered that she be discharged. Id. at 9.

Petitioner's expert, Dr. Souayah,[4] examined petitioner in November 2011. Pet'r's Ex. 21 at 1-2. Dr. Souayah diagnosed petitioner with "[s]tatus post [GBS], [p]ossible small-fiber neuropathy/large-fiber neuropathy" and "[p]ost [GBS] fatigue." Id. at 2.

III. Discussion

The Vaccine Act established the Program to compensate vaccine-related injuries and deaths. § 300aa-10(a). "Congress designed the Vaccine Program to supplement the state law civil tort system as a simple, fair and expeditious means for compensating vaccine-related injured persons. The Program was established to award 'vaccine-injured persons quickly, easily, and with certainty and generosity.'" Rooks v. Sec'y of Health & Human Servs., 35 Fed. Cl. 1, 7 (1996) (quoting H.R. Rep. No. 908 at 3, reprinted in 1986 U.S.C.C.A.N. at 6287, 6344).

A. Standards for Adjudication

Petitioner's burden of proof is a preponderance of the evidence. § 300aa-13(a)(1). The preponderance of the evidence standard, in turn, has been interpreted to mean that a fact is more likely than not. Moberly v. Sec'y of Health & Human Servs., 592 F.3d 1315, 1322 n.2 (Fed. Cir. 2010). Proof of medical certainty is not required. Bunting v. Sec'y of Health & Human Servs., 931 F.2d 867, 873 (Fed. Cir. 1991). A petitioner who satisfies this burden is entitled to compensation unless the government can prove, by a preponderance of the evidence, that the vaccinee's injury is "due to factors unrelated to the administration of the vaccine." § 300aa-13(a)(1)(B).

To receive compensation under the Program, petitioner must prove either: (1) that she suffered a "Table Injury"—i.e., an injury listed on the Vaccine Injury Table—corresponding to a vaccine that she received, or (2) that she suffered an injury that was actually caused by the HPV vaccine. See §§ 300aa-13(a)(1)(A) and 11(c)(1); Capizzano, 440 F.3d at 1319-20. Petitioner must show that the vaccine was "not only a but-for cause of the injury but also a substantial factor in bringing about the injury." Moberly, 592 F.3d at 1321 (quoting Shyface v. Sec'y of Health & Human Servs., 165 F.3d 1344, 1352-53 (Fed. Cir. 1999)).

B. Petitioner's Injury

The threshold issue in this case is whether petitioner had GBS. A determination of what afflicted petitioner "is a prerequisite to . . . [a causation] analysis." Broekelschen v. Sec'y of Health & Human Servs., 618 F.3d 1339, 1346 (Fed. Cir. 2010). For the reasons discussed below, the undersigned finds by a preponderance of the evidence that petitioner did have GBS.

[4] Dr. Souayah's credentials and qualifications are discussed in section III.D.i below.

i. Guillain-Barré syndrome

Guillain-Barré syndrome is "an acute, immune-mediated disorder of the peripheral nervous system." Resp't's Ex. H[5] at 1488. The syndrome is characterized by

> weakness and numbness or a tingling sensation in the legs and arms and possible loss of movement and feeling in the legs, arms, upper body, and face. It is frequently severe and usually presents as an ascending paralysis marked by weakness in the legs that spreads to the upper limbs and the face along with complete loss of deep tendon reflexes.

Pet'r's Ex. 22, Tab AAA,[6] at 220.

"GBS is a diverse disorder, including both demyelinating and axonal forms." Pet'r's Ex. 22, Tab FF,[7] at 389. "There is a marked patient to patient variation concerning the clinical features [of GBS], severity of the illness and electrodiagnostic findings." Pet'r's Ex. 22, Tab DDD,[8] at 342. Most GBS "[p]atients suffer from generalized weakness," as well as "varying degree[s] of sensory disturbances." Pet'r's Ex. 22, Tab G,[9] at 61. However, there are multiple subtypes of GBS that differ "mainly in terms of the pathological and electrodiagnostic features." Pet'r's Ex. 22, Tab BB,[10] at 605; see also Pet'r's Ex. 22, Tab CC,[11] at 578 (discussing clinically defined variants of GBS throughout the world with "prominent differences"). "[U]p to 20% of patients have normal [nerve] conduction studies." Resp't's Ex. H at 1488. "The CSF is normal in the first week of the illness." Pet'r's Ex. 22, Tab AAA, at 226. Thus, GBS generally requires a clinical diagnosis. See Transcript ("Tr.") at 105 (Dr. Souayah), 121 (Dr. Leist).

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[5] Antonino Uncini & Satoshi Kuwabara, "Electrodiagnostic criteria for Guillain-Barré syndrome: A critical revision and the need for an update," 123 Clinical Neurophysiology 1487 (2012).

[6] Anand B. Pithadia & Nimisha Kakadia, "Guillain-Barré syndrome (GBS)," 62 Pharmacological Reports 220 (2010).

[7] Tony Ho & John Griffin, "Guillain-Barré syndrome," 12 Current Opinion in Neurology 389 (1999).

[8] Martina M. Prendergast & Anthony P. Moran, "Lipopolysaccharides in the development of the Guillain-Barré syndrome and Miller Fisher syndrome forms of acute inflammatory peripheral neuropathies," 6:5 J. Endotoxin Research 341 (2000).

[9] C. Wim Ang et al., "The Guillain-Barré Syndrome: a true case of molecular mimicry," 25:2 TRENDS in Immunology 61 (2004).

[10] Vittorio Govoni & Enrico Granieri, "Epidemiology of the Guillain-Barré syndrome," 14 Current Opinion in Neurology 605 (2001).

[11] J.W. Griffin et al., "Guillain-Barré syndrome in northern China: The spectrum of neuropathological changes in clinically defined cases," 118 Brain 577 (1995).

GBS is commonly "associated with an antecedent infection within six weeks prior to symptom onset, generally an upper respiratory tract infection or gastroenteritis . . . In addition to antecedent infections, GBS develops after vaccination." Ex. 22, Tab AAA, at 221.

There are two diagnostic criteria for GBS – motor weakness and loss of deep tendon reflexes (DTRs). Tr. 16, 105-06; see Pet'r's Ex. 22, Tab Q,[12] at 163 (GBS is "marked by weakness in the legs that spreads to the upper limbs and the face along with complete loss of deep tendon reflexes."); see, e.g., Pet'r's Ex. 22, Tab R,[13] at 1630; Pet'r's Ex. 22, Tab U,[14] at 61; Pet'r's Ex. 22, Tab III,[15] at 45; Pet'r's Ex. 22, Tab P,[16] at 136; Pet'r's Ex. 22, Tab PP,[17] at 98.

In general, patients spontaneously recover, although recovery may be accelerated by IVIG treatment. Pet'r's Ex. 22, Tab G, at 61; see also Pet'r's Ex. 22, Tab MM,[18] at 162 (among others, IVIG "represent[s] the mainstay of . . . treatment of GBS"). Most patients have a favorable clinical course and complete recovery. Pet'r's Ex. 22, Tab BB, at 605. Despite a good recovery, many patients with GBS will have severe fatigue, which is "one of the most disabling symptoms." Pet'r's Ex. 22, Tab S,[19] at 2393.

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[12] Kei Funakoshi et al., "*Campylobacter coli* enteritis and Guillain-Barré syndrome: No evidence of molecular mimicry and serological relationship," 246 Journal of Neurological Sciences 163 (2006).

[13] Yoshiko Furiya et al., "Complete Recovery of an Aged Patient with Guillain-Barré Syndrome Associated with Multiple IgM Anti-Ganglioside Antibodies," 38 Muscle & Nerve 1630 (2008).

[14] M.P.J. Garssen et al., "Amantadine for treatment of fatigue in Guillain-Barré syndrome: a randomised, double blind, placebo controlled, crossover trial," 77 Journal of Neurology, Neurosurgery & Psychiatry 61 (2006).

[15] Eli Shahar, "Current Therapeutic Options in Severe Guillain-Barré Syndrome," 29:1 Clinical Neuropharmacology 45 (2006).

[16] Uwe Enders et al., "The Spectrum of Immune Responses to Campylobacter jejuni and Glycoconjugates in Guillain-Barré Syndrome and in Other Neuroimmunological Disorders," 34(2) Annals of Neurology 136 (1993).

[17] Marko Kutleša et al., "Acute Motor Axonal Neuropathy Associated with Pandemic H1N1 Influenza A Infection," 13 Neurocritical Care 98 (2010).

[18] Bernd C. Kieseier & Hans-Peter Hartung, "Therapeutic Strategies in the Guillain-Barré Syndrome," 23(2) Seminars in Neurology 159 (2003).

[19] M.P.J. Garssen et al., "Physical training and fatigue, fitness, and quality of life in Guillain-Barré syndrome and CIDP," 63 Neurology 2393 (2004).

ii. Petitioner's Evidence

Petitioner developed "a progressive ascending numbness and weakness in both lower extremities . . . consistent with the diagnosis of GBS." Pet'r's Ex. 22 at 9. But aspects of petitioner's clinical course were not classic for GBS in that she had asymmetric weakness and her diagnostic studies, including EMG, nerve conduction studies ("NCS"), and CSF studies were all normal. Dr. Souayah acknowledged that patients with GBS generally present with abnormal CSF findings. Tr. 106. Dr. Souayah maintains, however, that abnormal CSF results are not necessary to support a diagnosis of GBS. Tr. 106; see also Pet'r's Post-Hearing Br. at 28-29. Medical literature cited by petitioner also indicates that CSF results are "normal in the first week of the illness" and initial NCS studies are normal is 13% of patients. Pet'r's Ex. 22, Tab AAA, at 226.

Petitioner's treating physicians agree that she had GBS. Pet'r's Post-Hearing Br. at 33. Petitioner's neurologist, Dr. Angels, diagnosed petitioner with "possible GBS" on February 2, and "GBS . . . worsening over last 48 [hours]" on February 5, 2009. Pet'r's Ex. 13 at 56. Dr. Angels ordered IVIG treatment for petitioner due to her diagnosis of GBS. Id. Dr. Angels diagnosed petitioner with "probable" GBS on February 9, 2009. Id. at 47. And Dr. Angels's diagnosis on February 10, 2009, was GBS. See id. at 45, 231.

Petitioner's other treating physicians diagnosed her with GBS or at least seemingly deferred to other physicians' diagnoses of GBS. See Pet'r's Ex. 14 at 14 (Dr. Hutter's diagnosis was "Mild [GBS] . . . secondary to vaccination"); Pet'r's Ex. 20 at 6 (Dr. Kou's "personal findings are [patient] . . . with past history [of] GBS"); Pet'r's Ex. 8 at 12 (Dr. Adler's diagnosis was "acute . . . [GBS]"); Pet'r's Ex. 5 at 43 (Dr. Saphier noting petitioner's "history of [GBS]"); Pet'r's Ex. 20 at 8 (Dr. Miller noting petitioner's diagnosis of GBS in her medical history). The opinions of these treating physicians are afforded substantial weight. See Capizzano, 440 F.3d at 1326.

Dr. Souayah, petitioner's expert, also examined petitioner and reviewed her past medical records. See Pet'r's Ex. 26. According to Dr. Souayah, petitioner demonstrated the two diagnostic criteria for GBS, "weakness in the upper and lower extremities and reduced or absent deep tendon reflexes." Pet'r's Post-Hearing Br. at 27 (citing Tr. 16, 105-06). Petitioner had reduced and then absent reflexes, consistent with a diagnosis of GBS. Id. at 28. In Dr. Souayah's view, "ascending weakness is the hallmark of GBS," id. at 27, but "there can be asymmetrical weakness in some patients . . . [and] a patient can develop weakness only on one side." Id. at 27 n.14 (citing Tr. 46).

iii. Respondent's Evidence

Respondent asserts that petitioner failed to show that she had GBS. Resp't's Post-Hearing Br., filed Dec. 9, 2013, at 11-12. Respondent's expert, Dr. Thomas Leist,[20] disagreed that petitioner had GBS because her presentation was not "clear-cut." Tr. 119-20; see also tr. 120-24, 140; Resp't's Ex. A at 9-10. Specifically, Dr. Leist claims that petitioner's retained reflexes and asymmetrical weakness suggest that she did not suffer from GBS. Resp't's Ex. A at

[20] Dr. Leist's credentials and qualifications are discussed in section III.D.ii below.

9-10. Respondent also argues that petitioner's "rapid fluctuation of her motor function during her . . . five day hospitalization" is inconsistent with GBS. Resp't's Pre-Hearing Br. at 9. But Dr. Leist acknowledged that GBS is generally a clinical diagnosis and that he was "Monday morning quarterbacking" in petitioner's case. Tr. 144, 141.

Respondent also argues that petitioner's diagnosis of GBS is questionable because "none of petitioner's treating physicians diagnosed GBS unequivocally." Resp't's Post-Hearing Br. at 14 (citing Pet'r's Ex. 3 at 4). In spite of Dr. Leist's concerns with petitioner's diagnosis of GBS, he conceded that he did not "disagree with the working hypothesis [of GBS]" of petitioner's treating physicians. Tr. 141.

Respondent maintains that "no objective testing," namely, NCS, EMG, and CSF testing, confirmed petitioner's diagnosis of GBS. Resp't's Post-Hearing Br. at 13. According to respondent, petitioner's normal diagnostic test results are "highly atypical for someone with GBS." Id. at 12-14. Specifically, Dr. Leist asserted that petitioner's normal CSF results were inconsistent with a diagnosis of GBS. Tr. 154-55. Dr. Leist, however, acknowledged that some patients with GBS may have normal CSF results "very early in the disease." Tr. 156.

Dr. Leist proposed an alternative explanation for petitioner's symptoms, which was that petitioner suffered from small fiber neuropathy caused by her pre-existing health issues, including PCOS, obesity, and pre-diabetes. Tr. 125-26, 140; Resp't's Ex. A at 10-11. Dr. Leist acknowledged that none of petitioner's treating physicians diagnosed petitioner with small fiber neuropathy or suggested that her pre-existing health issues could have caused her neurological issues. Tr. 159-60.

iv. Evaluation of the Evidence

A preponderance of the evidence demonstrates that petitioner suffered from GBS. Petitioner complained of flu-like symptoms which progressed to paresthesia in her extremities on February 2, 2009.[21] On February 3, 2009, petitioner complained of acute numbness in all of her extremities. Pet'r's Ex. 10 at 3. These symptoms persisted and by February 5, 2009, petitioner had developed weakness in her lower extremities. Pet'r's Ex. 13 at 56. Petitioner received a five-day course of IVIG treatment ordered by her physicians for her diagnosis of GBS. Pet'r's Ex. 8 at 12. By February 10, 2009, she had symmetrical decreased sensation in her arms and legs. Id. at 9, 11. Petitioner exhibited generalized weakness and absent reflexes on February 10, 2009. Id. at 11.

All of these aspects of petitioner's clinical course are consistent with a diagnosis of GBS. This diagnosis is further supported by the fact that petitioner's treating physicians diagnosed her with GBS, as discussed above. See, e.g., Pet'r's Ex. 20 at 8, 9 (neurologist Dr. Ann Miller

[21] On February 2, 2009, petitioner presented to HUMC for increased weakness and paresthesias, which "had extended proximally to approximately the level of the knee . . . [then] extended to the thigh region as well as the upper extremities (right great[er] than left)." Pet'r's Ex. 12 at 21. Dr. Angels noted petitioner had paresthesias of all extremities, but had no significant weakness. Id. at 22.

noting petitioner's history of GBS on July 22, 2011). Although Dr. Noskin questioned in February 2010 whether petitioner's diagnosis of GBS was correct because of her "peculiar" symptoms, Dr. Noskin only suggested CIDP as a "possibility" and did not reject the diagnosis of GBS. See Pet'r's Ex. 3 at 4. Further, Dr. Noskin listed "polyneuropathy" as petitioner's "[p]rimary" diagnosis and ordered Lyrica to treat it. Id.

Accordingly, the undersigned finds that petitioner has provided preponderant evidence that she suffered from GBS. This finding is informed primarily by the opinions of petitioner's treating physicians, who consistently diagnosed petitioner with GBS. See Capizzano, 440 F.3d at 1326. It is further informed by the medical literature submitted by the parties, which supports petitioner's diagnosis of GBS.

C. Causation - Elements of Petitioner's Claim

The second issue to resolve is whether petitioner's GBS was caused by her HPV vaccine. Because petitioner does not allege that she suffered a Table injury, she must prove that the HPV vaccine she received caused her injury. To do so, she must establish, by preponderant evidence: (1) a medical theory causally connecting the vaccine and her injury ("Althen Prong One"); (2) a logical sequence of cause and effect showing that the vaccine was the reason for her injury ("Althen Prong Two"); and (3) a showing of a proximate temporal relationship between the vaccine and her injury ("Althen Prong Three"). Althen, 418 F.3d at 1278; § 300aa–13(a)(1) (requiring proof by a preponderance of the evidence).

Petitioner cannot establish entitlement to compensation based solely on her assertions. Rather, a vaccine claim award must be supported either by medical records or by the opinion of a competent physician. § 300aa-13(a)(1). In determining whether petitioner is entitled to compensation, the special master shall consider all material contained in the record, § 300aa-13(b)(1), including "any . . . conclusion, [or] medical judgment . . . which is contained in the record regarding . . . causation . . . of petitioner's illness." § 300aa-13(b)(1)(A). Thus, the undersigned must weigh the submitted evidence and the testimony of the parties' offered experts and rule in petitioner's favor when the evidence weighs in her favor. Moberly, 592 F.3d at 1325-26 ("Finders of fact are entitled—indeed, expected—to make determinations as to the reliability of the evidence presented to them and, if appropriate, as to the credibility of the persons presenting that evidence."); Althen, 418 F.3d at 1280-81.

D. The Parties' Experts

i. Petitioner's Expert, Nizar Souayah, M.D.

Dr. Souayah testified on petitioner's behalf. See Pet'r's Exs. 22 and 24.[22] Dr. Souayah received his undergraduate and medical school training in Tunisia and France. Pet'r's Ex. 23

[22] Respondent alleges that Dr. Souayah committed "extensive plagiarism" in preparing his initial report. Resp't's Post-Hearing Br. at 18 n.9; Resp't's Pre-Hearing Br. at 17. Respondent notes that a substantial portion of Dr. Souayah's initial report "included sentences and entire paragraphs copied directly from five [medical literature articles], in addition to his own previously published article." Resp't's Post-Hearing Br. at 18 n.9. Petitioner re-filed Dr.

(Dr. Souayah's curriculum vitae) at 1. He then completed a residency in family practice and primary care at the Medical School of Tunis, Tunisia, and a residency in internal medicine and vascular disease at the Hospitals of Medical School of Strasbourg, France. Id. He also completed a residency in neurology at Temple University in Philadelphia, Pennsylvania. Id. at 2. Afterward, he completed fellowships in neurology and the EMG lab/Neuromuscular unit at Harvard Medical School. Id. He completed another fellowship in axonal loss, neurogeneration, and neuroprotection at Drexel University Medical School in Philadelphia, Pennsylvania. Id. Dr. Souayah is currently a professor of neurology at New Jersey Medical and Dental School, where he also serves as the director of the Neuropathy Center and as program director of the Neuromuscular Medicine Program. Pet'r's Ex. 23 at 2-3; Tr. 7. He is the founder of the Peripheral Neuropathy Center and a neuromuscular fellowship. Tr. 7-8. Dr. Souayah is board-certified in neurology, neuromuscular medicine, psychiatry, and electrodiagnostic medicine. Tr. 12; Pet'r's Ex. 23 at 2. Dr. Souayah has published medical literature concerning vaccine-related adverse reactions. Tr. 10-11; Pet'r's Ex. 23 at 7-9. He is on the editorial board of three journals and serves as a reviewer for approximately 15-20 journals. Tr. 13-14.

In addition to teaching medical students and residents, Dr. Souayah has clinical responsibilities. Tr. 8. At the Peripheral Neuropathy Center, he sees patients with peripheral neuropathy conditions, such as GBS, CIDP, and diabetic neuropathy. Tr. 8. Dr. Souayah has extensive experience treating individuals with GBS. As he explained, "since 2004 . . . [a]ny single patient who was diagnosed [at New Jersey Medical and Dental School] with [GBS] . . . or suspicion of [GBS] . . . would come to see [him]." Tr. 9. He estimates that he sees approximately five to ten confirmed cases of GBS each year. Tr. 9, 37.

Dr. Souayah has had one patient with GBS that was associated with an HPV vaccination. Tr. 98-100. Another physician had diagnosed the patient with GBS. Tr. 99. Dr. Souayah saw that patient approximately two years after the onset of GBS, which began one week after HPV vaccination and peaked two or three weeks later. Tr. 99-100.

ii. Respondent's Expert, Thomas Leist, M.D.

Dr. Leist testified on behalf of respondent. Tr. 114. Dr. Leist received a Ph.D. in biochemistry and immunology from the University of Zurich. Resp't's Ex. F at 1; tr. 114. He completed a postdoctoral fellowship in immunology at the University of California at Los Angeles. Tr. 114. He received his medical degree from the University of Miami. Tr. 114. Dr. Leist completed a residency in neurology at Sloan Kettering New York Hospital and then completed a "combined research/clinical fellowship in neuroimmunology" at the National Institutes of Health. Tr. 115; Resp't's Ex. F at 1. He has been a professor of neurology at Thomas Jefferson University in Philadelphia, Pennsylvania, since 2000. Tr. 115; Resp't's Ex. F at 1. In that capacity, he is an attending physician and works with fellows and residents. Tr. 115. He spends approximately 65% of his time in his clinical practice and approximately 25%

Souayah's report with appropriate citations to the articles he referenced and clear indications of which parts of his report are attributable to other sources. See Pet'r's Ex. 22, re-filed July 2, 2013. Because Dr. Souayah's testimony in this case is consistent with the opinions held by petitioner's treating physicians, his failure to cite his sources in his initial expert report is not fatal to his opinions.

of his time conducting research. Tr. 115-16. He is board-certified in neurology and serves as an editor and peer-reviewer for medical journals. Tr. 116; Resp't's Ex. F at 1. He estimates that he sees three to six patients with GBS per year and has seen approximately 100 patients with GBS in his clinical practice. Tr. 117.

E. Althen Prong One: Petitioner's Medical Theory

Under Althen Prong One, petitioner must set forth a medical theory explaining how the received vaccine could have caused the sustained injury. Andreu v. Sec'y of Health & Human Servs., 569 F.3d 1367, 1375 (Fed. Cir. 2009). Under this prong, petitioner must make a showing that the received vaccine can cause the alleged injury. Pafford v. Sec'y of Health & Human Servs., 451 F.3d 1352, 1355-56 (Fed. Cir. 2006).

Petitioner's theory of causation need not be medically or scientifically certain, Knudsen v. Sec'y of Health & Human Servs., 35 F.3d 543, 548-49 (Fed. Cir. 1994), but it must be informed by "sound and reliable medical or scientific explanation." Id. at 548; see also Veryzer v. Sec'y of Health & Human Servs., 98 Fed. Cl. 214, 223 (2011) (noting that special masters are bound by both § 300aa-13(b)(1) and Vaccine Rule 8(b)(1) to consider only evidence that is both "relevant" and "reliable"). If petitioners rely upon a medical opinion to support their theory, the basis for the opinion and the reliability of that basis must be considered in the determination of how much weight to afford the offered opinion. See Broekelschen, 618 F.3d at 1347 ("The special master's decision often times is based on the credibility of the experts and the relative persuasiveness of their competing theories."); Perreira v. Sec'y of Health & Human Servs., 33 F.3d 1375, 1377 n.6 (Fed. Cir. 1994) ("An expert opinion is no better than the soundness of the reasons supporting it.") (citing Fehrs v. United States, 620 F.2d 255, 265 (Ct. Cl. 1980)).

i. Petitioner's Expert, Dr. Souayah

Dr. Souayah opines that petitioner's HPV vaccination caused her GBS. Pet'r's Ex. 22 at 9; tr. 15. GBS is thought to be a post-infectious autoimmune disorder, tr. 28, and in approximately two-thirds of cases, an upper respiratory or gastrointestinal infection is the suspected cause. Pet'r's Ex. 22 at 9. Dr. Souayah believes, however, that petitioner's "Gardasil vaccination, more probably than not, was the triggering factor for her GBS by a mechanism that is similar to the one triggered by upper respiratory or gastrointestinal infection." Id.

In his expert report, Dr. Souayah discusses several possible mechanisms thought to cause GBS, including but not limited to, molecular mimicry, a theory involving "perturbation of immunoregulatory mechanisms," and direct destruction of the myelin "by the vaccine virus or vaccine-associated products." Pet'r's Ex. 22 at 11. Dr. Souayah also suggested another possible mechanism whereby there was a "non-specific activation of the immune system by the Gardasil vaccine or one of the vaccine-associated products against the peripheral nerve" which caused petitioner's nerve damage. Id. Dr. Souayah also believes that petitioner's genetic profile or other factors of her immune system may have predisposed her to develop GBS after vaccination. Id.

Of the various possible mechanisms set forth in his expert report, Dr. Souayah opined that the mechanism of molecular mimicry was the most likely explanation for how petitioner's

HPV vaccination caused her GBS. Id. at 10-11. Dr. Souayah summarized his theory of molecular mimicry, as applied to petitioner, as follows:

> [The] Gardasil vaccination induced activation of [petitioner's] . . . immune system. Some of the antibodies produced by the immune system . . . against the vaccine, more probably than not, reacted with the myelin sheath of [petitioner's] . . . peripheral nervous system and cause[d] nerve damage. This reaction occurs because of the antigenic similarity between the vaccine or one of its component[s] with the myelin sheath (molecular mimicry).

Id. at 11; see also tr. 26-27.

According to Dr. Souayah, molecular mimicry is a "well documented" cause of GBS. Specifically, it is generally accepted as an explanation for how a number of infections can cause neurological injuries, including GBS. Tr. 26-27; see, e.g., Pet'r's Ex. 22, Tab AAA, at 222 ("The most commonly proposed mechanism for the development of autoimmune disease is molecular mimicry."). He opined that molecular mimicry has explained how certain infections and vaccines, including the HPV vaccine, can cause GBS. Tr. 27, 30-31; Pet'r's Ex. 22 at 10.

> Molecular mimicry is
>
> sequence and/or conformational homology[23] between an exogenous agent (foreign agent) and self-antigen leading to the development of tissue damage and clinical disease from antibodies and T cells directed initially against the exogenous agent that also react against the self-antigen.

Institute of Medicine, Adverse Effects of Vaccines: Evidence and Causality 70 (Kathleen Stratton et al. eds., 2012) ("IOM Report"); see also Pet'r's Ex. 22, Tab AAA, at 222 ("Molecular mimicry refers to the situation where the pathogen and host share nearly identical antigens, which induces an antibody and T cell immune response that is cross reactive."); Pet'r's Ex. 22, Tab FF, at 390 (molecular mimicry occurs when "the immune response to specific antigens in infectious organisms attack[s] similar epitopes in the host peripheral nervous system"); see also Pet'r's Ex. 22, Tab JJJ,[24] at 308 (molecular mimicry is "an immune response to an infectious organism [that] results in immune attack on an epitope shared by the organism and nerve fibers"). Thus, Dr. Souayah stated that there must be some homology between the components of a vaccine and a component of the human body for molecular mimicry to occur. Tr. 63.

Dr. Souayah conceded, however, that there is no evidence that the HPV vaccine shares homology with any component of the human body. Tr. 63, 64, 92. Further, he acknowledged that petitioner was not tested for evidence of molecular mimicry. Tr. 63. But Dr. Souayah

[23] Homology is "the morphological identity of corresponding parts; structural similarity due to descent from a common form." Dorland's at 868.

[24] K.A. Sheikh et al., "Molecular Mimicry in Guillain-Barré Syndrome," 845 Annals of New York Academy of Science 307 (1998).

opined that the HPV vaccine could cause GBS via molecular mimicry based on "extrapolation" from other studies. Tr. 63. Specifically, Dr. Souayah opined that studies strongly suggest that the *Campylobacter jejuni* ("*c. jejuni*") bacteria can cause GBS via molecular mimicry. See tr. 63, 64, 92; see also Pet'r's Ex. 22, Tab AAA, at 222; Tr. 168 (Dr. Leist stating that "there is evidence clearly linking infections to molecular mimicry").

Dr. Souayah referenced numerous medical articles[25] in support of his theory. The Borja-Hart study reported on 13 cases of GBS that occurred after receipt of the HPV vaccine, as identified by searching the Vaccine Adverse Event Reporting System (VAERS). Pet'r's Ex. 22, Tab J;[26] Pet'r's Ex. 22 at 12-13. Of those 13 cases reported, 7 (53.8%) patients had received "concomitant vaccination with the meningococcal vaccine, which has been associated with GBS…the average time to onset of symptoms from the date of vaccination ranged from 1 to 82 days . . . In 6 of the reports, HPV vaccine was administered solely." Pet'r's Ex. 22, Tab J, at 357-58. The authors concluded that, while they "are unable to show any causality between the HPV vaccine and any of the serious adverse effects reviewed here[,] [i]t is critical, however, for healthcare providers to remain vigilant and continue to report any adverse effects following vaccines to a reporting system." Id. at 358.

Another article discusses a study Dr. Souayah and his colleagues authored about whether the HPV vaccine can cause GBS. Tr. 31-32 (discussing Pet'r's Ex. 31[27]). In that study, Dr. Souayah and his colleagues used VAERS data as well as data from the Center for Biologics and Research. Pet'r's Ex. 31 at 1. A "board-certified neuromuscular specialist . . . identif[ied] events that met the diagnostic criteria of GBS defined by progressive arm and leg weakness and areflexia" between June 2006 and September 2009. Pet'r's Ex. 31 at 1. The authors found 69 reported cases of GBS after vaccination with Gardasil. Id. at 2; tr. 32. The authors also found that the incidence of GBS after vaccination with HPV is "much higher" in the first six weeks after HPV vaccination, especially within the first two weeks. Tr. 32-33; see also tr. 73.

Dr. Souayah further explained that GBS

> is not occurring more often after HPV vaccination than it does in the general population. However, the fact that most of these cases occurred within 6 weeks of vaccination does warrant careful monitoring for any additional cases and continued analysis.

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[25] See Pet'r's Post-Hearing Br., App'x Index of Petitioner's Medical Literature, filed Dec. 9, 2013. The undersigned has considered the entire record. § 300aa-13(a)(1). However, only evidence relevant to resolution of this matter will be discussed. See Paterek v. Sec'y of Health & Human Servs., 527 Fed. App'x 875, 884 (Fed. Cir. 2013).

[26] Borja-Hart et al., "Human Papillomavirus Vaccine Safety in Pediatric Patients: An Evaluation of the Vaccine Adverse Event Reporting System," 43 Annals of Pharmacotherapy 356 (2009).

[27] Nizar Souayah et al., "Guillain-Barré syndrome after Gardasil vaccination: Data from Vaccine Adverse Event Reporting System (2006-2009)," Vaccine (2010) ("Souayah Article").

Resp't's Ex. I at 2. Dr. Souayah does not assert that his study's findings establish a cause and effect relationship, but rather he is "calling for more controlled studies" due to the study's findings and findings of similar studies. Tr. 33-34; see also tr. 56-57.

ii. Respondent's Expert, Dr. Leist

Dr. Leist disagreed with Dr. Souayah that the HPV vaccine can cause GBS via molecular mimicry. See Resp't's Ex. A at 7-9; tr. 129-33. He based his opinion, in part, on the lack of evidence of homology between a component of the HPV vaccine and a part of the human body. Tr. 168-69. Dr. Leist acknowledged, however, that 100% homology is not necessary for molecular mimicry to occur. Tr. 169.

Dr. Leist agreed that animal models have documented GBS being caused via molecular mimicry and that "there is evidence clearly linking infections to molecular mimicry." Tr. 168. But he opined that there is no indication that the HPV vaccine can cause GBS. Tr. 129. Dr. Leist testified that the fact that a live HPV does not cause GBS suggests that the HPV vaccine does not cause it either. Tr. 131. Dr. Leist also noted that the Institute of Medicine ("IOM") did not find evidence of HPV causing GBS via molecular mimicry. Tr. 133 (discussing Resp't's Ex. B[28] at 3); see also Resp't's Ex. A at 7-8. Further, he agreed with Dr. Souayah that no tests were performed on petitioner to determine whether her GBS was a response to her HPV vaccine. See tr. 169-72; see also IOM Report at 70 (explaining why "[p]roving that a particular human autoimmune disease is due to molecular mimicry is problematic").

Dr. Leist opined that multiple epidemiological studies that both he and Dr. Souayah reference show that there is no causal relationship between the HPV vaccine and GBS. Resp't's Ex. A at 9.[29] Dr. Leist criticized Dr. Souayah's reliance on VAERS data due to its limitations. Resp't's Ex. A at 8 (quoting Pet'r's Ex. 22, Tab UUU[30] at 291 ("The numerous acknowledged limitations of VAERS including underreporting, selective reporting, lack of a control group, inadequate denominator data to calculate event rates and diagnostic uncertainty of events result in the presence of strong biases in VAERS data.")). According to Dr. Leist, VAERS data has inherent biases, which make studies that utilize it less reliable. Tr. 138. Dr. Leist conducted an extensive critique of the other medical literature on which Dr. Souayah relied. In his view, none of the medical literature supports Dr. Souayah's opinion that the HPV vaccine can cause GBS via molecular mimicry. See Resp't's Ex. A at 11-23.

[28] IOM Report at 511.

[29] Citing IOM Report at 511-12; Pet'r's Ex. 22, Tab J.

[30] Frederick Varricchio et al., "Understanding vaccine safety information from the Vaccine Adverse Event Reporting System," 23 J. Pediatric Infectious Disease 287 (2004).

iii. Evaluation of the Evidence

The undersigned finds that petitioner has provided preponderant evidence that the HPV vaccine can cause GBS via molecular mimicry. Accordingly, petitioner has satisfied Althen Prong One.

Dr. Leist agreed with Dr. Souayah's opinion that molecular mimicry is a generally accepted theory in other contexts. Specifically, the parties' experts both opined that molecular mimicry is a well-documented explanation for how a *c. jejuni* infection can cause GBS. See tr. 26 (Dr. Souayah), 168 (Dr. Leist). Although Dr. Souayah conceded that there is no medical literature that demonstrates homology between the HPV vaccine and a component of the body, he opines that "extrapolation" from other studies documenting molecular mimicry provides a basis for his opinion that the HPV vaccine can induce GBS via molecular mimicry. See tr. 63-64. "[T]o require identification and proof of specific biological mechanisms would be inconsistent with the purpose and nature of the vaccine compensation program." Knudsen, 35 F.3d at 549. Therefore, "a paucity of medical literature supporting a particular theory of causation cannot serve as a bar to recovery." Andreu, 569 F.3d at 1379 (citations omitted).

F. Althen Prong Two: Logical Sequence of Cause and Effect

Under Althen Prong Two, petitioner must prove "a logical sequence of cause and effect showing that the vaccination was the reason for [her] injury." Althen, 418 F.3d at 1278. This requires petitioner to show that the vaccine she received actually caused the alleged injury. Pafford, 451 F.3d at 1354. Petitioner need not make a specific type of evidentiary showing. That is, petitioner is not required to offer "epidemiologic studies, rechallenge, the presence of pathological markers or genetic disposition, or general acceptance in the scientific or medical communities to establish a logical sequence of cause and effect." Capizzano, 440 F.3d at 1325. Instead, petitioner may satisfy her burden by presenting circumstantial evidence and reliable medical opinions. See id. at 1325-26.

i. Petitioner's Expert, Dr. Souayah

Dr. Souayah opined that petitioner was healthy before receipt of the HPV vaccine on January 27, 2009. Pet'r's Ex. 22 at 9. Petitioner subsequently developed GBS. Id. Prior to vaccination, she did not have any signs of an acute antecedent illness, such as "influenza infection, upper respiratory or gastrointestinal infection" that could have triggered her GBS. Pet'r's Ex. 22 at 9, Tr. 35-36.

Because petitioner did not have an antecedent upper respiratory or gastrointestinal infection within six weeks prior to symptom onset, Dr. Souayah concluded that "[t]he Gardasil vaccination, more probably than not, was the triggering factor for her GBS by a mechanism that is similar to the one triggered by upper respiratory or gastrointestinal infection in non-vaccination GBS patients." Id. In Dr. Souayah's opinion, the vaccine triggered the "immunological reaction that causes GBS by molecular mimicry." Id. at 11. Specifically, some of the antibodies produced by petitioner's immune system against the Gardasil vaccine, "more probably than not, reacted with the myelin sheath of her peripheral nervous system and cause[d]

nerve damage. This reaction occurs because of the antigenic similarity between the vaccine or one of its components with the myelin sheath (molecular mimicry)." Id.

Dr. Souayah also testified that petitioner's clinical course was consistent with vaccine-induced GBS. Pet'r's Ex. 22 at 16-17. Shortly after her HPV vaccination, she developed a number of symptoms consistent with GBS. Specifically, on approximately February 2, 2009, petitioner had weakness and reduced reflexes, which Dr. Angels "documented objectively." Tr. 21. Petitioner received IVIG treatment and her symptoms of weakness improved. Tr. 22. But by February 10, 2009, petitioner's deep tendon reflexes were absent, which is typical of GBS. Tr. 39.

ii. Petitioner's Treating Physicians

Three of petitioner's treating physicians affirmatively documented that her HPV vaccine was the likely cause of her GBS. Dr. Hutter diagnosed petitioner with "[m]ild [GBS] . . . secondary to [HPV] vaccination" on February 2, 2009. Pet'r's Ex. 13 at 207. Dr. Angels, a neurologist, opined that petitioner's condition was "[p]robable GBS related to recent [HPV] vaccine" on February 9, 2009. Id. at 47. Likewise, Dr. Verrico ordered a VAERS report on February 3, 2009, which stated, "[complains of] fatigue [and] flu[] like symptoms starting few hours after administration of Gardasil." Pet'r's Ex. 1 at 3. On March 11, 2009, Dr. Verrico noted that she discussed with Merck representative regarding "details of [reaction] [to Gardasil]." Pet'r's Ex. 1 at 25.

Dr. Souayah also examined petitioner and agreed with her treating physicians' opinions that her HPV vaccine caused her GBS. Pet'r's Ex. 21 at 2. None of petitioner's other physicians disagreed with these diagnoses.[31] Although these diagnoses are not conclusive evidence of causation, see § 300aa-13(b)(1)(B), they provide strong support for petitioner's claim that the HPV vaccine caused her GBS. See Capizzano, 440 F.3d at 1326.

iii. Respondent's Expert, Dr. Leist

Respondent's expert, Dr. Leist suggested that petitioner suffered from small fiber neuropathy caused by her pre-existing health issues, but acknowledged that none of petitioner's treating physicians diagnosed petitioner with small fiber neuropathy or suggested that her pre-existing health issues could have caused her neurological problems. Tr. 125-26, 140, 159-60; Resp't's Ex. A at 10-11. Moreover, Dr. Leist conceded that none of petitioner's pre-existing health issues can cause GBS:

> [The Court] Dr. Leist . . . going back to the issues of prediabetes, obesity and polycystic ovary syndrome, you're not suggesting that obesity causes GBS, is that correct?

[31] Dr. Noskin questioned whether petitioner's symptoms were vaccine-related or were caused by something else. See Pet'r's Ex. 3 at 9 ("[r]eversible causes, such as . . . diabetic causes of neuropathy, also need to be considered"). Dr. Noskin suggested that other potential causes "need[ed] to be considered," id., but she did not reject the opinions of petitioner's other treating physicians who considered petitioner's GBS to be vaccine-related.

[Dr. Leist] No, I do not.
Q. You're not suggesting that polycystic ovary syndrome causes GBS, are you?
A. I do not.
Q. And you're not suggesting that a prediabetes condition causes GBS, are you?
A. No, I do not. Just as a remark, obviously, in diabetic patients, the risk for GBS is higher than in the general population.
[. . .]
Q. Okay.
A. I'm referring here solely with respect to the risks of a polyneuropathy.
Q. Okay. But I want the record to be clear, you're not suggesting that any of these conditions caused GBS?
A. No, that's not my testimony.

Tr. 179-80.

Moreover, the medical literature Dr. Leist cited in support of his theory that petitioner's neurological issues are attributable to her pre-existing health issues is largely irrelevant. According to Dr. Leist, the authors of the Ylitalo article[32] found that obese patients "have a higher risk of developing peripheral neuropathy." Tr. 134. The article, however, described a longitudinal study that tracked chronic changes in women for a period of twelve years. Resp't's Ex. C at 1. Its conclusions are not applicable to the facts of this case where petitioner had an episode of acute weakness with loss of reflexes.

Dr. Leist opined that the Randeva article[33] shows that there are a number of "risk factors that arise out of [PCOS]" that "could be linked to a peripheral nerve disease." Tr. 135. The article, however, discusses the relationship between PCOS and, among other things, glucose disorders, diabetes, thrombotic illnesses, and cardiovascular disease. Resp't's Ex. D at 1. The article does not discuss HPV, GBS, or small fiber neuropathy, and it is not relevant to the material issues in dispute in this case.

Likewise, Dr. Leist asserted that the Tabak article[34] demonstrates that "patients with a prediabetic state or with a state of glucose intolerance" can have an increased risk for peripheral nerve disease. Tr. 136. Although the article does discuss the relationship between prediabetes and small fiber neuropathy, Resp't's Ex. E at 1, petitioner was not diagnosed with prediabetes or diabetic neuropathy. Application of the findings discussed in the article to the facts of this case would be a stretch.

[32] Resp't's Ex. C, Kelly R. Ylitalo et al., "Serial anthropometry predicts peripheral nerve dysfunction in a community cohort," Diabetes Metab. Res. Rev., doi: 10.1002/dmmr.2367 (2012).

[33] Resp't's Ex. D, Harpal S. Randeva, "Cardiometabolic Aspects of the Polycystic Ovary Syndrome," 33(5) Endrocrine Reviews 812 (2012).

[34] Resp't's Ex. F, Adam G. Tabak et al., "Prediabetes: a high-risk state for diabetes development," 379 Lancet 2279 (2012).

Dr. Leist discussed the findings of the Gee article[35] and correctly pointed out that the authors found, among other things, "one case of GBS that was identified after the quadrivalent papilloma vaccine." Tr. 136-37; see Resp't's Ex. G at 8282. This finding supports petitioner's case. But the authors also concluded that the study "had limited power to assess associations between HPV4 and very rare adverse events such as GBS." Resp't's Ex. G at 8283.

iv. Evaluation of the Evidence

The opinions of petitioner's treating physicians who opined that her HPV vaccine caused her GBS are "quite probative" as treating physicians are in the "best position" to determine the cause of petitioner's condition. Capizzano, 440 F.3d at 1326. Respondent argues that petitioner's treating physicians performed a "simplistic examination of the temporal relationship between the vaccine and subsequent illness, and apparent absence of a proven alternate cause," Resp't's Post-Hearing Br. at 21, to conclude that petitioner's HPV vaccine caused her GBS. Even if this were the case, that would not render their opinions insufficient to satisfy Althen Prong Two. See Andreu, 569 F.3d at 1376 ("A treating physician may rely on the close temporal proximity between a vaccine and an injury in concluding that there is a logical sequence of cause and effect between the vaccine and injury.").

The opinions of petitioner's treating physicians would be insufficient under Althen Prong Two had they merely noted a temporal relationship between petitioner's HPV vaccination and the onset of her GBS. See Moberly, 592 F.3d at 1323 (holding opinions of petitioner's treating physicians noting a temporal proximity insufficient under Althen Prong Two because none "drew a causal link" between vaccine and alleged injury). However, petitioner's treating physicians affirmatively and consistently opined that petitioner's HPV vaccine caused her GBS. Furthermore, Dr. Verrico recommended that petitioner not receive the second and third doses of the HPV vaccine. The undersigned finds that the opinions of Dr. Souayah and petitioner's treating physicians that her HPV vaccine caused her GBS are sufficient to satisfy her burden under Althen Prong Two.

G. Althen Prong Three: Medically Acceptable Timeframe

Under Althen Prong Three, petitioner must establish that her injury occurred within a timeframe that is medically acceptable for the alleged mechanism of harm. Althen, 418 F.3d at 1278. Petitioner satisfies this prong by producing "preponderant proof that the onset of symptoms occurred within a timeframe for which, given the medical understanding of the disorder's etiology, it is medically acceptable to infer causation-in-fact." de Bazan v. Sec'y of Health & Human Servs., 539 F.3d 1347, 1352 (Fed. Cir. 2008); see also Pafford, 451 F.3d at 1358 ("Evidence demonstrating petitioner's injury occurred within a medically acceptable timeframe bolsters a link between the injury alleged and the vaccination at issue under the 'but-for' prong of the causation analysis.").

[35] Resp't's Ex. G, Julianne Gee et al., "Monitoring the safety of quadrivalent human papillomavirus vaccine: Findings from the Vaccine Safety Datalink," 29 Vaccine 8279 (2011).

The parties dispute the onset of petitioner's GBS. Petitioner maintains that she "developed the onset of symptoms attributable to GBS between February 2 and February 5, 20[09], approximately seven to ten days after her HPV vaccination." Pet'r's Post-Hearing Br. at 46 (citing tr. 34, 50-51).[36] Respondent asserts the onset of petitioner's GBS occurred within hours after her vaccination when she experienced "diarrhea, likely within a few hours after the vaccine," and fatigue, chills, aches, "tingling in her feet" and lower legs approximately one day after vaccination. Resp't's Post-Hearing Br. at 21 (citing Pet'r's Ex. 1 at 22).

i. Petitioner's Expert, Dr. Souayah

Dr. Souayah opined that the onset of petitioner's symptoms related to her GBS began "between seven to ten days after the administration with HPV," which was approximately "between February 2nd and February 5th, [2009]." Tr. 34. In Dr. Souayah's opinion, petitioner's "objective weakness" and "reduc[tion] of deep tendon reflexes" documented by Dr. Angels's physical examination on February 5, 2009, were the first symptoms of her GBS. Tr. 34, 48-49; see also Pet'r's Ex. 24 at 2-3. Dr. Souayah considered this timeframe to be a medically acceptable interval for his theory of molecular mimicry. Tr. 35; Pet'r's Ex. 24 at 2-3. Dr. Souayah opined that, as stated in the Govoni article, "[w]eakness can develop acutely (within days) or subacutely (up to 4 weeks)" in GBS cases. Pet'r's Ex. 22, Tab BB, at 605. "About two-thirds of GBS cases occur several days or weeks after"[37] a triggering event, such as an infection or a vaccination, and an increased risk of GBS within six to eight weeks after the flu vaccine has been documented. Pet'r's Ex. 22, Tab AAA, at 221.

Dr. Souayah refuted Dr. Leist's opinion that petitioner's "flu-like" symptoms and the "tingling" that she described in her lower extremities on January 29, 2009, were the first manifestations of GBS. Tr. 50-51. While Dr. Souayah acknowledged that tingling can be present in GBS, he disagreed that tingling is a specific characteristic of GBS. Tr. 106. He testified that tingling is a "subjective symptom" that can occur with other types of disorders, such as neuropathy, catatonic syndrome, radiculopathy, spinal cord disorders, and even heightened anxiety. Tr. 106-07. In Dr. Souayah's view, "[i]t is common to experience constitutional symptoms following vaccination," such as the fatigue, chills, aches, diarrhea and flu-like symptoms petitioner exhibited. Pet'r's Ex. 24 at 1. He considers these symptoms to be part of petitioner's "general, non-specific reaction to the vaccine" and that petitioner's "tingling did not constitute demyelination of the peripheral nerves." Id. at 1-2. And at the time that petitioner first complained of tingling, she did not have weakness or loss of reflexes. Tr. 50.

According to Dr. Souayah, the symptoms petitioner exhibited approximately one to two days after her vaccination, namely, tingling in her lower extremities, would constitute an onset of GBS that was too soon after her vaccination to be medically acceptable according to his theory of molecular mimicry. Tr. 52.

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[36] Petitioner inadvertently wrote "February 5, 2010" in her brief instead of "February 5, 2009."

[37] Pet'r's Ex. 22, Tab DD, Penina Haber et al., "Vaccines and Guillain-Barré Syndrome," 32(4) Drug Safety 309 (2009), at 1.

Dr. Souayah filed medical literature in support of his position that petitioner's symptom of tingling was too vague to constitute onset and that her symptom of weakness marked the onset of her GBS. In the Pithadia article, the clinical course of GBS is described as having three phases, initial, plateau and recovery. Pet'r's Ex. 22, Tab AAA, at 9. The initial phase of GBS "begins when the first definitive symptom develops." Id. A definitive or "major neurological sign" is "muscle weakness" which generally occurs first in the legs. Id.

ii. Respondent's Expert, Dr. Leist

Dr. Leist disagrees with Dr. Souayah that the onset of petitioner's symptoms is medically appropriate. Tr. 126-28. Dr. Leist is equivocal as to exactly when the onset of petitioner's neurological symptoms occurred. In his report, Dr. Leist suggested that the first symptom of petitioner's injury occurred "within hours" after her vaccination when she experienced "dysesthesia, tingling or abnormal sensation in her feet." Resp't's Ex. A at 9; see also Tr. 150. Likewise, Dr. Leist testified that petitioner's neurological symptoms first manifested either "within hours of the vaccine administration or . . . on the same day as the vaccine administration." Tr. 128.

Later in his testimony, however, Dr. Leist opined that petitioner's medical records were ambiguous as to timing and provided only an "approximate" timeframe for when petitioner's symptoms occurred. See tr. 152. Dr. Leist stated that petitioner's first symptom of a neurological injury was the "dysesthesia, tingling or abnormal sensation in her feet," which occurred "within hours" after petitioner received her HPV vaccine. Tr. 150. But he then stated that petitioner's "tingling" occurred "approximately 24 hours" after petitioner's HPV vaccine. Tr. 152. Thus, Dr. Leist's opinion is that petitioner's symptom onset occurred either within hours of her HPV vaccine or approximately twenty-four hours after her HPV vaccine. Both he and Dr. Souayah agree that the process of molecular mimicry could not produce GBS within 24 hours. Tr. 34, 128.

iii. Evaluation of the Evidence

The undersigned finds that the onset of petitioner's GBS occurred on approximately February 2, 2009, when petitioner presented to the ED with complaints of extremity weakness. On that date, petitioner's treating physician, Dr. Hutter, diagnosed her with mild GBS, and Dr. Angels suspected GBS. Prior to that date, petitioner did not have definitive symptoms or weakness. Thus, a preponderance of the evidence demonstrates that the onset of petitioner's GBS occurred approximately one week after her HPV vaccination.

Petitioner asserts that this timeframe is medically acceptable according to Dr. Souayah's theory of molecular mimicry. Pet'r's Post-Hearing Br. at 45. The medical literature also provides support for Dr. Souayah's opinion that approximately one week after the triggering event is an acceptable timeframe for GBS to occur. Pet'r's Ex. 22, Tab BB, at 605; Tab AAA, at 221.

Additionally, three of petitioner's treating physicians opined that petitioner's HPV vaccine was the likely cause of her GBS. In coming to this conclusion, they presumably found

that the timing of the onset of petitioner's GBS was medically acceptable to infer causation. See Contreras v. Sec'y of Health & Human Servs., 107 Fed. Cl. 280, 299 (2012) ("[I]t is difficult to conceive of a treating physician who would conclude that a vaccine caused a petitioner's illness without also concluding that the onset of the illness was within a medically-acceptable time-frame.").

H. Alternative Causation

Because petitioner has established a prima facie case, she is entitled to compensation unless respondent can put forth preponderant evidence "that [her] injury was in fact caused by factors unrelated to the vaccine." Whitecotton v. Sec'y of Health & Human Servs., 17 F.3d 374, 376 (Fed. Cir. 1994), rev'd on other grounds sub nom., Shalala v. Whitecotton, 514 U.S. 268 (1995); see also Walther v. Sec'y of Health & Human Servs., 485 F.3d 1146, 1151 (Fed. Cir. 2007).

In his report, Dr. Leist opined that petitioner's "[o]besity, [PCOS] . . . and insulin resistance, glucose intolerance, and prediabetes independently or in combination can explain [petitioner's] . . . progressive sensory complaints." Resp't's Ex. A at 11. According to respondent, however, "Dr. Leist is not suggesting that any of these conditions . . . can cause GBS . . . . Rather, he opines that petitioner appears to have suffered from these conditions, which have been associated with the type of progressive sensory complaints that petitioner experienced." Resp't's Post-Hearing Br. at 15 n.7.[38]

As discussed above, a preponderance of the evidence establishes that petitioner's neurological symptoms were symptoms of GBS, not symptoms of her pre-existing health issues, as Dr. Leist suggests.[39] More importantly, respondent and Dr. Leist do not assert that any of petitioner's pre-existing health conditions can cause GBS. See id.; tr. 179. Accordingly, respondent has failed to provide preponderant evidence of an alternative cause of petitioner's GBS.

[38] In her pre-hearing brief, respondent asserted that petitioner's "medical records support an alternate cause of petitioner's condition." Resp't's Pre-Hearing Br. at 18 (emphasis omitted). But in her post-hearing brief, respondent does not firmly argue that there is an alternative cause to petitioner's injuries. Rather, respondent argues that "respondent's evidence, including evidence of a potential alternative cause, is relevant to determining whether petitioner has established a prima facie case." Resp't's Post-Hearing Br. at 9.

[39] The undersigned notes that Dr. Noskin stated that "[r]eversible causes, such as . . . diabetic causes of neuropathy, also need[ed] to be considered." Pet'r's Ex. 3 at 9. But Dr. Noskin (and petitioner's other treating physicians) did not affirmatively attribute petitioner's neurological complications to her pre-existing health conditions.

IV. Conclusion

For the reasons discussed above, the undersigned finds that petitioner is entitled to compensation because she has provided sufficient circumstantial evidence that preponderates in her favor. A separate damages order will issue.

IT IS SO ORDERED.

s/ Nora Beth Dorsey
Nora Beth Dorsey
Special Master